

Attorney Docket No.: **ISPH-0524**
Inventors: **Bennett et al.**
Serial No.: **09/734,847**
Filing Date: **December 12, 2000**
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The following listing of claims will replace all prior versions and listings of claims in this application.

Listing of Claims:

Claims 1-33 (canceled).

Claim 34 (currently amended): A method of modulation of processing of a selected wild-type cellular mRNA target, said method comprising binding to said wild-type cellular mRNA target an antisense compound having at least one 2'guanidinium, 2'carbamate, 2'aminoxy, or 3'methylene phosphonate, or peptide nucleic acid (P.A.) modification, provided that when the antisense compound has at least one peptide nucleic acid modification (P.A.), the C terminus of said antisense compound has at least one arginine or lysine residue conjugated thereto; wherein said antisense compound is specifically hybridizable with said mRNA target and does not elicit cleavage of the mRNA target upon binding, so that processing of said mRNA target is modulated.

Claim 35 (previously presented): The method of claim 34 wherein said modulation of the processing of a selected wild-type cellular mRNA target is modulation of splicing of said mRNA target.

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Claim 36 (previously presented): The method of claim 34 wherein said antisense compound has a 2'guanidinium, 2'-acetamido, 2'carbamate, 2'aminoxy, or 2'-dimethylaminoethoxyethoxy modification on substantially every sugar.

Claim 37 (previously presented): The method of claim 36 wherein said antisense compound has at least one phosphorothioate backbone linkage.

Claim 38 (previously presented): The method of claim 34 wherein said antisense compound is an antisense oligonucleotide.

Claim 39 (previously presented): The method of claim 35 wherein said modulation of splicing is a redirection of splicing.

Claim 40 (previously presented): The method of claim 35 wherein said modulation of splicing results in an altered ratio of splice products.

Claim 41 (previously presented): The method of claim 35 wherein said modulation of splicing results in exclusion of one or more exons from a mature mRNA.

Claim 42 (previously presented): The method of claim 41 wherein said antisense compound is targeted to at least a portion of an exon to be excluded.

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Claim 43 (previously presented): The method of claim 42 wherein said antisense compound is targeted to an intron-exon junction.

Claim 44 (previously presented): The method of claim 39 wherein said antisense compound is targeted to at least a portion of a region up to 50 nucleobases upstream from a 5' splice site.

Claim 45 (previously presented): The method of claim 44 wherein said redirection of splicing is a decreased frequency of use of said 5' splice site.

Claim 46 (previously presented): The method of claim 34 wherein said processing of a selected wild-type cellular mRNA target is polyadenylation of said mRNA target.

Claim 47 (previously presented): The method of claim 34 wherein said antisense compound is targeted to a polyadenylation signal or polyadenylation site.

Claim 48 (previously presented): The method of claim 34 wherein said processing of a selected wild-type cellular mRNA target is regulating stability of said mRNA target, by targeting said antisense compound to a sequence which controls the stability of said mRNA target.

Claim 49 (previously presented): The method of claim 34 wherein said antisense compound which does not elicit cleavage of

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Claim 55 (previously presented)): The method of claim 53 wherein said modified backbone linkages alternate with phosphodiester and/or phosphorothioate backbone linkages.

Claim 56 (previously presented): The method of claim 53 wherein every backbone linkage is a modified backbone linkage other than a phosphorothioate linkage.

Claim 57 (currently amended): The method of claim 53 wherein said modified backbone linkage is a 3'-methyl phosphonate or peptide nucleic acid, provided that when the modified backbone linkage is a peptide nucleic acid, the C-terminus of said antisense compound has at least one arginine or lysine residue conjugated thereto.

Claim 58 (previously presented): The method of claim 34 wherein said antisense compound which does not elicit cleavage of the mRNA target upon binding contains at least one modified nucleobase.

Claim 59 (previously presented): The method of claim 57 wherein said modified nucleobase is a C-5 propyne.

Claim 60 (previously presented): The method of claim 40 wherein said altered ratio of splice products results from an increase or a decrease in the amount of a splice product encoding

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the mRNA target upon binding contains at least one modification which increases binding affinity for the mRNA target and which increases nuclease resistance of the antisense compound.

Claim 50 (previously presented): The method of claim 34 wherein said antisense compound which does not elicit cleavage of the mRNA target upon binding contains at least one nucleoside having a 2' modification of its sugar moiety.

Claim 51 (previously presented): The method of claim 50 wherein every nucleoside of said antisense compound has a 2' modification of its sugar moiety.

Claim 52 (previously presented): The method of claim 50 wherein said 2' modification is selected from the group consisting of 2'guanidinium, 2'-acetamido, 2'carbamate, 2'aminoxy, and 2'-dimethylaminoethoxyethoxy.

Claim 53 (previously presented): The method of claim 34 wherein said antisense compound which does not elicit cleavage of the mRNA target upon binding contains at least one modified backbone linkage other than a phosphorothioate backbone linkage.

Claim 54 (previously presented): The method of claim 53 wherein said antisense compound also contains at least one phosphodiester or phosphorothioate backbone linkage.

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a membrane form of a protein relative to a soluble form of a protein.

Claim 61 (previously presented): The method of claim 59 wherein said protein is a receptor.

Claim 62 (previously presented): The method of claim 60 wherein said receptor is a hormone or cytokine receptor.

Claim 63 (currently amended): The method of claim 34 wherein said antisense compound has a 3'-methyl phosphonate or peptide nucleic acid at substantially every backbone linkage, provided that when the antisense compound has a peptide nucleic acid at substantially every backbone linkage, the C-terminus of said antisense compound has at least one arginine or lysine residue conjugated thereto.